Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

A cerebral lymphoma mimicking a meningioma: case report

Imane Joudar, MD[a,b,*], Siham Nasri, PhD[a,b,c], Narjisse Aichouni, PhD[a,b], Imane Kamaoui, PhD[a,b], Imane Skiker, PhD[a,b,c]

Introduction: Cerebral lymphoma is a rare and aggressive brain tumor. It accounts for 1% of all non-Hodgkin's lymphomas (NHL) and 2% of all brain tumors. Untreated brain lymphoma has a very poor prognosis, with an overall life expectancy of around 1.5 months.

Case presentation: The authors report the case of a 35-year-old patient, with no previous pathological history, who presented for 3 weeks with deafness and recently aggravated otalgia. In MRI, brain imaging revealed a formation initially suggestive of an aggressive meningioma, and the histological study of the operative specimen was in favor of a diffuse large-cell non-germ-center B NHL.

Clinical discussion: Primary central nervous system lymphoma is an extra-nodal NHL localized to the brain, meninges, spinal cord, and eyes. In 90% of cases, these are diffuse large B-cell lymphomas, the other types being poorly characterized low-grade lymphomas, T-cell lymphomas, and Burkitt's lymphomas. MRI with gadolinium contrast is the gold standard for diagnosis which enhancement is homogeneous and well-limited, frequently associated with perilesional vascular edema. In T2-weighted sequences, there is a weak signal with restricted diffusion on diffusion-weighted imaging. The management of brain lymphoma is currently based on chemotherapy with high-dose methotrexate combined with the other agents, mainly rituximab.

Conclusion: Cerebral lymphoma remains a non-negligible entity of central nervous system tumors, which can be confused with several other tumors, mainly glial and meningioma.

Keywords: chemotherapy, extra-nodal lymphoma, MRI brain imaging, neurotoxicity, primary CNS lymphoma

Introduction

Cerebral lymphoma is a rare and aggressive brain tumor. It accounts for 1% of all non-Hodgkin's lymphomas (NHL) and 2% of all brain tumors. The incidence of this disease is rising sharply, especially in people over 65. This can be explained on the one hand by the use of immunosuppressive drugs either in the context of solid organ transplantation, chronic inflammatory disease, or active neoplasia and on the other hand, by incidental detection during the performance of imaging examinations for the surveillance of another disease. Untreated brain lymphoma has a very poor prognosis, with an overall life expectancy of around 1.5 months[1].

HIGHLIGHTS

- Cerebral lymphoma is a rare and aggressive brain tumor. It accounts for 1% of all non-Hodgkin's lymphomas and 2% of all brain tumors.
- In 90% of cases, these are diffuse large B-cell lymphomas, the other types being poorly characterized low-grade lymphomas, T-cell lymphomas, and Burkitt's lymphomas.
- MRI with gadolinium contrast is the gold standard for diagnosis, in which enhancement is homogeneous and well-limited, frequently associated with perilesional vascular edema.
- The management of brain lymphoma is currently based on chemotherapy with high-dose methotrexate combined with the other agents, mainly rituximab.

In this case, we report on a young, immunocompetent patient who presented with neurological symptoms, in whom brain imaging revealed a formation initially suggestive of an aggressive meningioma, and in whom the histological study of the operative specimen was in favor of a diffuse large-cell non-germ-center B non-Hodgkin's lymphoma.

Case presentation

We report the case of a 35-year-old female patient with no previous pathological history, who presented for 3 weeks with a recently aggravated and neglected left unilateral otalgia and deafness. The evolution was marked by the appearance of

[a]Faculty of Medicine and Pharmacy, Mohammed First University, [b]Department of Radiology, Mohammed VI University Hospital, Mohammed First University and [c]Faculty of Medicine and Pharmacy, Mohammed First University, LAMCESM, Oujda, Morocco

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Mohammed First University, Oujda, Morocco. Tel.: +212 11 53 78 05. E-mail: imane.joudar.ts@gmail.com (I. Joudar).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Medicine & Surgery (2023) 85:5100–5104

Received 5 June 2023; Accepted 22 July 2023

Published online 4 August 2023

http://dx.doi.org/10.1097/MS9.0000000000001126

headaches with vomiting in favor of an intracranial hypertension syndrome resistant to the usual antalgic drugs, which motivated the patient to consult the emergency department. On admission, the patient was hemodynamically and respiratory stable and conscious, with no sensory or motor deficits, neck stiffness, a VAS 6/10 headache, and no fever. Laboratory tests on admission were normal. A non-injected brain computed tomography scan was performed (Fig. 1), showing a spontaneously hyperdense and partially hypodense left temporal mass measuring 48×40 mm with extension to the parietal lobe and perilesional vasogenic edema, leading to the initial suspicion of a meningioma. A complementary cerebral MRI coupled with Angio sequences was performed (Fig. 2), showing a left fronto-temporal extra-axial tumoral process, in T1 hyposignal and T2 hypersignal, as well as a diffusion hypersignal, with an apparent diffusion coefficient (ADC) of 0.6×10^{-3}, and enhanced after gadolinium injection with a T1 hypersignal, meningeal contrast, and significant peri-injury edema, without rupture of the blood–brain barrier, all responsible for temporal and sub-falcoral engagement, with a right deviation of the midline measuring 13 mm. Atypical meningioma was considered, but lymphomatosis could not be excluded given the restricted diffusion. A lumbar puncture was not performed, given the presence of temporal engagement on imaging.

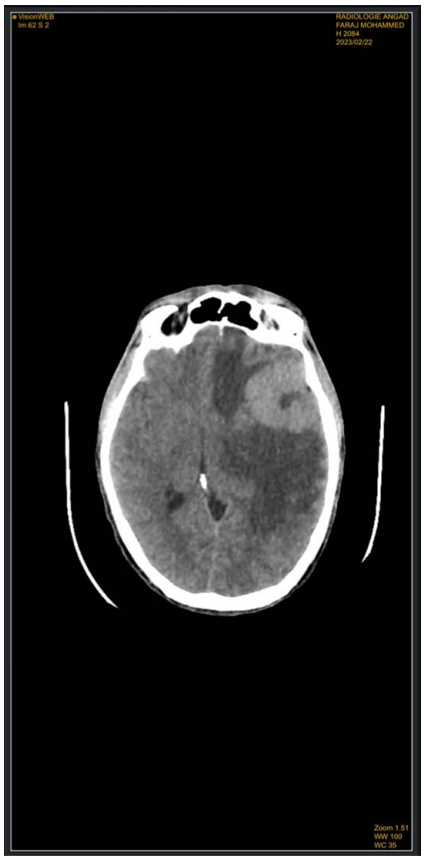

Figure 1. Noninjected cerebral computed tomography scan showing a spontaneously hyperdense, partially hypodense left temporal mass measuring 48×40 mm with extension to the parietal lobe with perilesional vasogenic edema.

The patient underwent surgical excision of the tumor, with a simple postoperative course and a friable, grayish-white macroscopic appearance, with a few foci of hemorrhagic remodeling.

Microscopic examination revealed a dense, diffuse proliferation of round lymphomatous cells, with large tumor cells with basophilic cytoplasm. Immunohistochemistry showed positive staining for anti-CD20 antibody, 90% for anti-Ki67 antibody, and anti-MUM1 antibody, in favor of diffuse large-cell non-Hodgkin's B lymphoma without germinal center. The patient was referred to the oncohematology center, and after a multidisciplinary discussion, the patient was put on a protocol associating high-dose methotrexate (MTX) with targeted radiotherapy. After 4 months after the start of the protocol, the patient is behaving well, with a functional amelioration in terms of auditory function and a minor persistency of headaches, which are controlled by analgesics to this day.

The Surgical CAse REport (SCARE) Guidelines were used in the writing of this paper[2].

Discussion

Primary central nervous system lymphoma (PCNSL) is an extranodal NHL localized to the brain, meninges, spinal cord, and eyes. It accounts for around 2% of all primary central nervous system tumors, with the overall incidence of PCNSL increasing, particularly in the older patient population[3].

In 90% of cases, these are diffuse large B-cell lymphomas (DLBCL), the other types being poorly characterized low-grade lymphomas, T-cell lymphomas, and Burkitt's lymphomas. Advances in molecular biology have provided new insights into the pathogenesis of cerebral lymphomas. Recurrent and frequent mutations of the B-cell receptor, and its target NFκB, remain the basis of the genesis of large B-cell lymphomas[4].

Clinically, the patient usually presents with symptoms of sensory-motor deficit, symptoms of intracranial hypertension syndrome, cognitive or behavioral disorders. In other rare cases, the patient may present with reduced visual acuity secondary to ocular localization or spinal cord involvement[5].

MRI with gadolinium contrast is the gold standard for diagnosis. Firstly, enhancement is homogeneous and well-limited, frequently associated with perilesional vascular edema. In T2-weighted sequences, there is a weak signal with restricted diffusion on diffusion-weighted imaging, which is explained by high cellularity and a high nuclear/cytoplasmic ratio. These characteristics differentiate it from other cerebral tumors, mainly gliomas, tumoral demyelinating lesions, and meningiomas[6].

It should be noted that ADC values are inversely correlated with cytopathological progression of PCNSL cell density and may be a prognostic factor[7]. Several data suggest that pretherapeutic ADC measurements in the contrast-taking lesion are predictive of overall survival in immunocompetent patients treated with a combination of high-dose MTX and rituximab[8].

MRI plays an important role in the differential diagnosis, which is made primarily with glioblastoma, the difference between which is made by the heterogeneous nature of the enhancement with a central necrotic zone in high-grade glioma, as well as a hyperintense signal on ADC, and the fact that cortical involvement is more frequent than in lymphomas[9].

Other imaging techniques differentiate lymphomas from other glial tumors, such as the fractional anisotropy of diffusion tensor imaging, which correlates with the myelinated fibers'

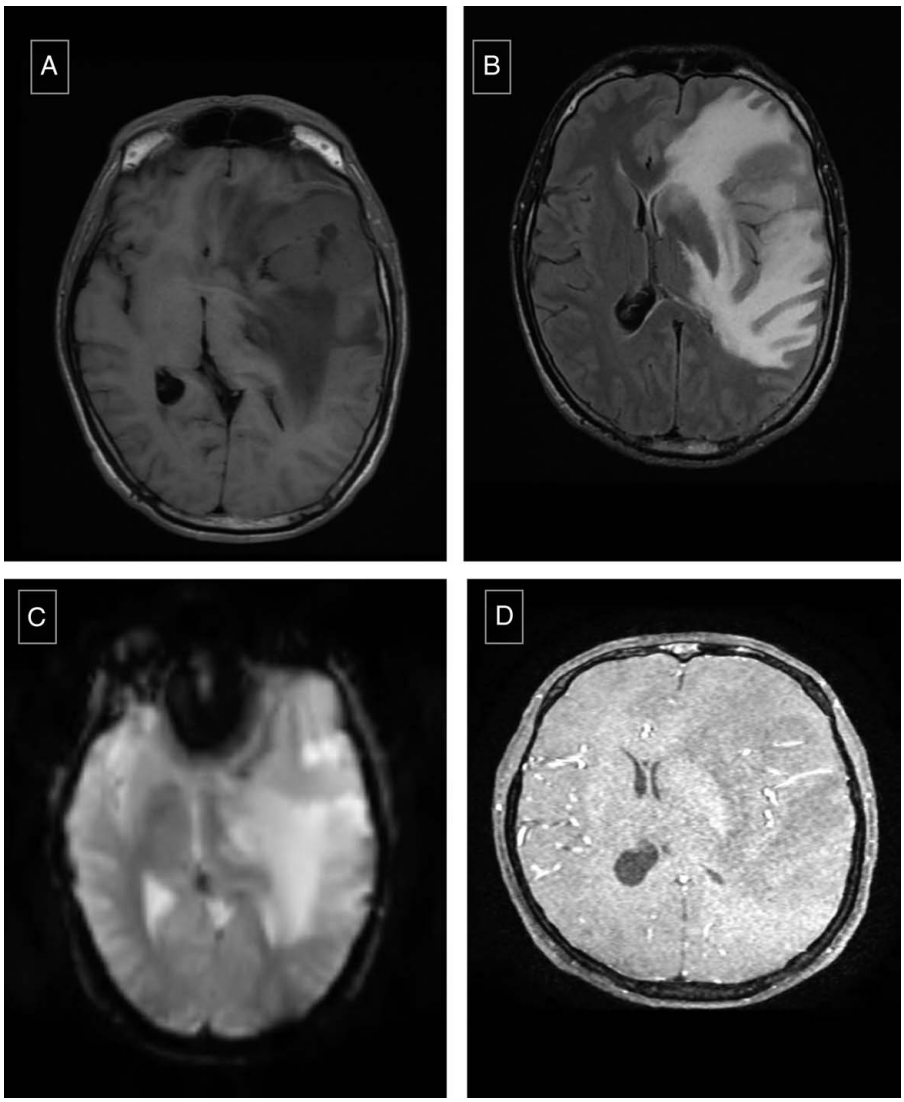

Figure 2. Cerebral MRI shows an extra-axial tumoral process with heterogeneous lobulated contours in T1 hyposignal (A), which enhances after injection of gadolinium (D), and in T2 hypersignal (B), and diffusion hypersignal with an ADC measured at 0.6×10^{-3}(C).

microstructural integrity and is notably lower in PCNSL than in glioblastoma multiforme[9]. Added to this is the role of metabolic imaging by positron emission tomography in predicting response to treatment at a very early phase, as well as in detecting early relapse of the disease during follow-up treatment. These imaging techniques can play an important role in the close monitoring of patients to predict response to treatment and to individualize short-term and long-term follow-up[9].

PCNSL presents as an isolated brain tumor in up to 70% of immunocompetent patients, with a preferential localization in the supratentorial region and a predominance of periventricular white substance. The disease is rarely limited to the cerebrospinal fluid (CSF), eye, or spinal cord at the time of diagnosis[3]. The gold standard for diagnosis is a histological analysis of the mass or, failing that, a stereotactic biopsy fragment. In certain situations, CSF studies, flow cytometry, or chorioretinal biopsy may help in the diagnosis, but with a diagnostic delay compared with stereotactic biopsy. An important diagnostic step is to confirm the primary nature of cerebral lymphoma, as opposed to systemic NHL with secondary brain involvement[3].

For this purpose, contrast-enhanced MRI of the spine, slit-lamp examination of both eyes, and CSF analysis are essential, with testicular ultrasound for men, as 3% of men with testicular lymphoma have brain metastases at the time of diagnosis.

The management of brain lymphoma is currently based on chemotherapy with two phases, which differ in terms of protocol and objectives. The induction phase aims to achieve a complete radiographic response, while the consolidation phase aims to eliminate all residual diseases and improve overall prognosis[10].

Since 1970, high-dose MTX has been considered the most effective treatment for cerebral lymphoma, with overall response rates of 35–74%, median progression-free survival of 10–12.8 months and median overall survival of 25–55 months. These results were improved by combining MTX with other agents, mainly temozolomide, rituximab, and procarbazine[11,12].

A retrospective study by Chen *et al*.[13], comparing two chemotherapy induction protocols between MTX-HD plus temozolomide (MT group) and MTX-HD combined with rituximab and temozolomide (RMT group). Objective responses were observed in 93.7% of patients in the RMT group and 69.0% of patients in the MT group ($P = 0.018$), while complete responses were observed in 53.2% of patients in the RMT group and 27.6% of patients in the MT group ($P < 0.001$). The overall survival rates at 2 and 5 years were 65.7 and 50.0%, respectively, for the MT group and 82.3 and 82.3% for the RMT group ($P = 0.015$).

A multicenter phase 2 trial evaluated a combined protocol of HD-MTX, procarbazine, vincristine, and rituximab (RMPV), followed by reduced-dose consolidating WBRT and cytarabine[14]. Comprehensive neuropsychological testing in this study demonstrated an improvement in both executive function and verbal memory after induction chemotherapy due to tumor response and relatively stable scoring at 48 months follow-up.

Radiation therapy was historically the mainstay of treatment for brain lymphoma due to its high sensitivity to radiation until the efficacy of MTX became apparent, although radiotherapy did achieve high initial responses but with early relapse in the majority of patients. Another problem is related to late neurotoxicity, which is a real challenge in survivors, particularly in patients over 60 years of age[15]. Due to inadequate disease control and the risk of neurotoxicity, radiotherapy alone is no longer routinely indicated for the treatment of brain lymphoma[15].

The role of surgery in lymphoma treatment remains controversial. It may be limited to histopathological diagnosis by stereotactic biopsy. However, there is some evidence of an overall prognostic benefit of surgical resection over biopsy[16]. On the other hand, surgical resection can be deleterious, especially in terms of neurological deficits, but in certain situations, it remains indispensable, especially in the presence of intracranial hypertension or spinal cord compression[17]. In these rare cases, tumor debulking can be beneficial, improving symptoms and tolerance to future intensive chemotherapy[18].

In view of its increasing incidence and poor prognosis, and following the efficacy of protocols combining high-dose MTX with autologous stem cell transplantation in postinduction consolidation, replacing whole-brain radiotherapy is associated with a high risk of late neurotoxicity. At present, new treatments such as Bruton tyrosine kinase inhibitors and chimeric antigen receptor T cells (CAR-T) have shown efficacy and good overall tolerability in PCNSL patients, opening up promising therapeutic prospects for improving overall survival and functional prognosis in these patients.

Conclusion

Cerebral lymphoma remains an important tumor of the central nervous system, with a markedly increasing incidence in the elderly. It can be confused with several other tumors, mainly glial and meningeal, but brain MRI with metabolic and diffusion imaging techniques remains an important noninvasive tool for diagnostic orientation. Current treatment is mainly based on high-dose MTX-based chemotherapy combined with agents such as rituximab and temozolomide, as well as high-dose MTX with autologous stem cell transplantation in postinduction consolidation[17].

Ethical approval

The ethical committee approval was not required, given the article type (case report). However, the written consent to publish the clinical data of the patients was given and is available to check by the handling editor if needed.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

I.J.: first author who contributed to this research in writing up and collating data; S.N.: second author who contributed to the study concept, data analysis, and collection; N.A., I.K., and I.S.: supervised and validated the final version.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

This is not an original research project involving human participants in an interventional or observational study but a case report. This registration was not required.

Guarantor

Dr Imane Joudar.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

Not available.

References

[1] Batchelor TT. Primary central nervous system lymphoma: a curable disease. Hematol Oncol 2019;37(S1):15–8.
[2] Agha RA, Franchi T, Sohrabi C, *et al*. and SCARE Group. The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84:226–30.
[3] Han CH, Batchelor TT. Diagnosis and management of primary central nervous system lymphoma. Cancer 2017;123:4314–24.
[4] Tsang M, Cleveland J, Rubenstein JL. On point in primary CNS lymphoma. Hematol Oncol 2020;38:640–7.
[5] Wang C-C, Carnevale J, Rubenstein JL. Progress in central nervous system lymphomas. Br J Haematol 2014;166:311–25.

[6] Barajas RF, Politi LS, Anzalone N, *et al*. Consensus recommendations for MRI and PET imaging of primary central nervous system lymphoma: guideline statement from the International Primary CNS Lymphoma Collaborative Group (IPCG). Neuro Oncol 2021;23:1056–71.
[7] Raguž M, Mudrovčić Y, Dlaka D, *et al*. Primary dural lymphoma mimicking meningioma: a clinical and surgical case report. J Surg Case Rep 2018;2018:rjy189.
[8] Saini J, Kumar Gupta P, Awasthi A, *et al*. Multiparametric imaging-based differentiation of lymphoma and glioblastoma: using T1-perfusion, diffusion, and susceptibility-weighted MRI. Clin Radiol 2018;73:986.e7–15.
[9] Ambady P, Hu LS, Politi LS, *et al*. Primary central nervous system lymphoma: advances in MRI and PET imaging. Ann Lymphoma 2021;5:27.
[10] Rubenstein JL, Hsi ED, Johnson JL, *et al*. Intensive chemotherapy and immunotherapy in patients with newly diagnosed primary CNS lymphoma: CALGB 50202 (Alliance 50202). J Clin Oncol 2013;31:3061–8.
[11] Yamanaka R, Homma J, Sano M, *et al*. Salvage immuno-chemotherapy with a combination of rituximab, high-dose cytarabine, mitoxantrone and dexamethasone for patients with primary CNS lymphoma: a preliminary study. Leuk Lymphoma 2007;48:1429–33.
[12] Doorduijn JK, van Imhoff GW, van der Holt B, *et al*. Treatment of secondary central nervous system lymphoma with intrathecal rituximab, high-dose methotrexate, and R-DHAP followed by autologous stem cell transplantation: results of the HOVON 80 phase 2 study. Hematol Oncol 2017;35:497–503.
[13] Chen C, Sun P, Cui J, *et al*. High-dose Methotrexate plus temozolomide with or without rituximab in patients with untreated primary central nervous system lymphoma: a retrospective study from China. Cancer Med 2019;8:1359–67.
[14] Glass J, Won M, Schultz CJ, *et al*. Phase I and II study of induction chemotherapy with methotrexate, rituximab, and temozolomide, followed by whole-brain radiotherapy and postirradiation temozolomide for primary CNS lymphoma: NRG Oncology RTOG 0227. J Clin Oncol 2016;34:1620–5.
[15] Ferreri AJM. Therapy of primary CNS lymphoma: role of intensity, radiation, and novel agents. Hematology Am Soc Hematol Educ Program 2017;2017:565–77.
[16] Correia CE, Schaff LR, Grommes C. Central nervous system lymphoma: approach to diagnosis and treatment. Cancer J 2020;26:241–52.
[17] Hoang-Xuan K, Bessell E, Bromberg J, *et al*. Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology. Lancet Oncol 2015;16:e322–32.
[18] Calimeri T, Steffanoni S, Gagliardi F, *et al*. How we treat primary central nervous system lymphoma. ESMO Open 2021;6:100213.